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Ocular Irritation Evaluation with Eye Wash Regimen of Liquid Propellant 1846

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MAMMALIAN TOXICOLOGY BRANCH
DIVISION OF TOXICOLOGY

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Toxicology Series: 199

LETTERMAN ARMY INSTITUTE OF RESEARCH
PRESIDIO OF SAN FRANCISCO, CALIFORNIA 94129

Ocular Irritation Evaluation with Eye Wash Regimen of Liquid Propellant 1846 (Toxicology Series 199)--Justus and Korte

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In conducting the research described in this report, the investigation adhered to the "Guide for the Care and Use of Laboratory Animals," as promulgated by the Committee on Revision of the Guide for Laboratory Animal Facilities and Care, Institute of Laboratory Animal Resources, National Research Council.

This material has been reviewed by Letterman Army Institute of Research and there is no objection to its presentation and/or publication. The opinions or assertions contained herein are the private views of the author(s) and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense. ***(AR 360-5)***

for Richard A. Kaschmitt 29 Apr 88

Edwin S. Beatrice (date)
COL, MC
Commanding

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LP1846 is a liquid propellant under development by the U.S. Army for potential use in a 155-mm self-propelled howitzer. The purpose of this study was to determine whether LP1846 is an ocular irritant, and if so, whether flushing the eye with water 10 seconds or 30 seconds after exposure will reduce the ocular toxicity. The compound was tested in the laboratory rabbit.

The result of this study indicate that LP1846 is an ocular irritant in accordance with test criteria of the Environmental Protection Agency. Observations included conjunctival redness, chemosis, iritis, corneal opacities, and neovascularization of the cornea. All lesions were reversible except for the neovascularization. Washing the eye at 30 seconds alleviated the conjunctival and iritic symptoms and prevented the development of corneal lesions. Immediate washing at 10 seconds was even more successful at alleviating the symptoms. However, even after washing, the ocular irritation potential of LP1846 was sufficient to produce an irritant response according to test criteria.

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ABSTRACT

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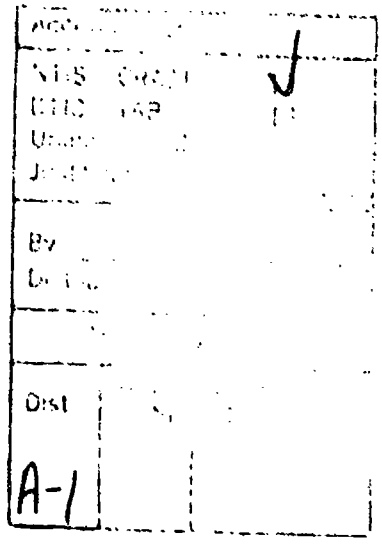
Key Words: Primary Eye Irritation, Liquid Propellant, LP1846, Rabbit, HAN, TEAN, Nitrates



PREFACE

TYPE REPORT: Primary Eye Irritation GLP Study Report

TESTING FACILITY:
US Army Medical Research and Development Command
Letterman Army Institute of Research
Presidio of San Francisco, CA 94129-6800

SPONSOR:
US Army Medical Research and Development Command
US Army Biomedical Research and Development Laboratory
Fort Detrick, MD 21701-5010
Project Officer: Robert Finch, PhD

PROJECT/WORK UNIT/APC: USAMBRDL Reimbursable Service Order 8620/F844, Project Order 86PP6823 (BASIC), TL2R

GLP STUDY NUMBER: 86006

STUDY DIRECTOR: MAJ Don W. Korte Jr, PhD, MSC

PRINCIPAL INVESTIGATOR: James D. Justus, BS, MPA, SSG, USA

PATHOLOGIST: CPT Charles B. Clifford, DVM, VC

REPORT AND DATA MANAGEMENT:
A copy of the final report, study protocol, retired SOPs, raw data, analytical, stability, and purity data of the test compound, tissues, and aliquot of the test compound will be retained in the LAIR Archives.

TEST SUBSTANCE: LP1846

INCLUSIVE STUDY DATES: 18 Feb - 5 Apr 1988

OBJECTIVE: The objective of this study was to determine the primary eye irritation potential of LP1846 and the effect of washing after instillation of the compound, in male New Zealand White rabbits.

ACKNOWLEDGMENTS

SP4 Dean Magnuson, BS, SP4 Villmar O. Villa, BS, CPT Denzil Frost, DVM, and CPT Gary Zaucha, DVM, assisted in the research; SGT Barb Green, Richard Katona, and Charlotte Speckman provided animal care; SGT Gayle A. Orner provided manuscript assistance; and Andre Ackers provided photographic expertise. Special thanks to MAJ LuAnn McKinney, DVM, for answering numerous questions on rabbit ophthalmology.

SIGNATURES OF PRINCIPAL SCIENTISTS AND MANAGERS INVOLVED IN THE STUDY

We, the undersigned, declare that GLP Study 86006 was performed under our supervision, according to the procedures described herein, and that this report is an accurate record of the results obtained.

Don W. Korte Jr. 28 Sep 88

DON W. KORTE JR., PhD / DATE
MAJ, MSC
Study Director

James D. Justus 28 Sept 88

JAMES D. JUSTUS, BS, MPA / DATE
SSG, USA
Principal Investigator

Conrad R. Wheeler 28 Sep 88

CONRAD R. WHEELER, PhD / DATE
CAC
Analytical Chemist

DEPARTMENT OF THE ARMY

LETTERMAN ARMY INSTITUTE OF RESEARCH
PRESIDIO OF SAN FRANCISCO, CALIFORNIA 94129-6800

REPLY TO
ATTENTION OF:

SGRD-ULZ-QA (70-1n) 27 September 1988

MEMORANDUM FOR RECORD

SUBJECT: GLP Compliance for GLP Study 86006

1. This is to certify that in relation to LAIR GLP Study 86006, the following inspections were made:

17 July 1986	-	Protocol Review
24 February 1988	-	Animal Receipt
01 March 1988	-	Dosing
02 March 1988	-	Observations/Scoring
07 March 1988	-	Weighing
16 March 1988	-	Necropsy
17 March 1988	-	Test Chemical Log

2. The institute report entitled "Ocular Irritation Evaluation with Eye Wash Regimen of Liquid Propellant 1846," Toxicology Series 199, was audited on 12 September 1988.

Carolyn M. Lewis
CAROLYN M. LEWIS
Chief, Quality Assurance

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Ocular Irritation Evaluation with Eye Wash Regimen of Liquid Propellant 1846 -- Justus and Korte

INTRODUCTION

Liquid propellants are being evaluated by the Armed Forces because they offer several important advantages over conventional solid propellants. They are much less expensive to produce and transport, less vulnerable to secondary ignition, easier to store in combat vehicles, and demilitarized simply and safely (1). Since there is considerable potential for human contact with liquid propellants during manufacture, transportation, and use, their effects on human health are of primary concern to the Army. One of the most promising liquid propellant mixtures is LP1846, a mixture of hydroxylammonium nitrate, triethanolammonium nitrate, and water. The Army plans to use LP1846 to fire 155-mm shells from a howitzer by 1990 (2).

NOS-283, a monopropellant developed for the Navy and similar to LP1846 in composition, has been shown to be an ocular irritant (3). Therefore, one of the primary concerns with fielding LP1846 is the effect of accidental or inadvertent ocular exposure of the weapon's crew. If one member of the weapon's crew were disabled by a temporary reduction in visual acuity due to accidental exposure to LP1846, it would significantly reduce the combat effectiveness of the crew. Consequently, it was necessary to define the ocular toxicity associated with LP1846 exposure in a well-defined model and to determine the effect of washing on the severity and duration of the ocular effects.

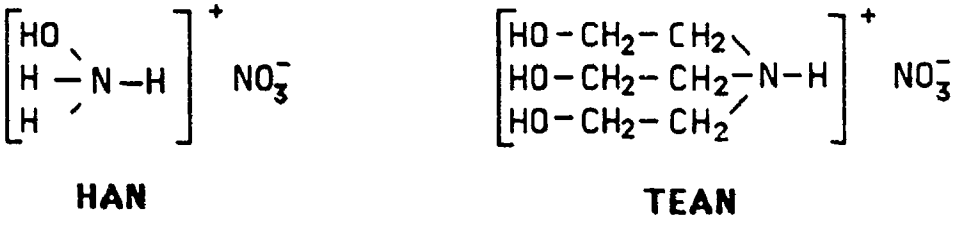
Objective of Study

The objective of this study was to determine the primary eye irritation potential of LP1846, and the effect of washing after instillation of the compound, in male New Zealand White rabbits.

MATERIALS

Test Substance

LP1846 (Lot #50-4) was obtained from Charles Leveritt at the United States Army Ballistics Research Laboratory (Aberdeen Proving Ground, MD). LP1846 is a mixture that contains 60.5% hydroxylammonium nitrate (HAN), 18.4% triethanolammonium nitrate (TEAN), and 20.1% water (Fig. 1). Additional chemical data are presented in Appendix A.



HAN TEAN

Figure 1. Components of LP1846

Vehicle

None

Animal Data

Twenty male New Zealand White rabbits (Hazleton Research Products, P.O. Box 7200, Denver, PA) were identified individually by writing numbers in their ears with indelible ink. Two animals were used for quality controls. The animal weights on dosing day ranged from 2.6 kg to 3.4 kg. Additional animal data appear in Appendix B.

Husbandry

The rabbits were housed individually in stainless steel, battery-type cages with automatically flushing dumptanks and screened bottoms (no bedding). The diet consisted of approximately 150 g per day of Certified Purina Chow Diet 5322 (Ralston Purina Company, Checkerboard Square, St. Louis, MO); purified water was provided from a Technic Series 300 Reverse Osmosis Unit (Seattle, WA) through a central line. The animal room temperature was maintained at 68°F to 72°F with a relative humidity range of 40 to 61%. The photoperiod was 12 hours of light per day.

METHODS

This study was conducted in compliance with the Good Laboratory Practices (GLP) regulations promulgated by the Environmental Protection Agency (EPA)(4) and LAIR SOP-OP-STX-33 (5). Letterman Army Institute of Research (LAIR) is an animal care facility approved by the American Association for Accreditation of Laboratory Animal Care (AAALAC). All research conformed with standards established in the Institute of Laboratory Animal Resources (ILAR) Guide for the Care and Use of Laboratory Animals and with other appropriate

federal regulations.

Group Assignment/Acclimation

Study rabbits were assigned to one of three groups: the No-Wash Group, the Wash-at-10-Seconds Group, and the Wash-at-30-Seconds Group. The animals were acclimated for at least 11 days before the dosing. During this period they were observed daily for signs of illness. The animals were checked for signs of ocular abnormalities upon arrival and 24 hours before dosing.

Dosage Levels

One-tenth milliliter (145.5 $\pm$ 0.2 mg) of LP1846 was instilled into one eye of each rabbit by gently pulling the lower lid away from the conjunctival cul-de-sac to form a cup into which the compound was placed. The upper and lower lids were then gently held together for one second to prevent the loss of material.

Compound Preparation

LP1846 was administered neat; therefore no compound preparation was required.

Test Procedures

On the day before dosing, each rabbit was observed for overall health status, and both eyes were evaluated first by unaided visual examination, then with the slit lamp, and finally after application of fluorescein dye for any corneal, iridial, or conjunctival abnormalities. The left eye was chosen for dosing unless an abnormality was observed, in which case the right eye was used. Animals with significant ocular abnormalities were removed from the study.

Washing was accomplished by gently flushing the treated eye with tap water at room temperature. The wash period was 60 seconds in duration, and approximately 80 ml of water was used for the wash. For one group of animals, the treated eye was washed beginning 30 seconds after the compound was instilled. For the second group, the treated eye was washed beginning 10 seconds after the compound was instilled.

Observations

The ocular reactions were graded and scored in accordance with the schedule in Table I. Observations were made at 1, 4, 24, 48, and 72 hours, and 7, 14, and 21 days after dosing or until the treated eye had cleared, whichever came first. Fluorescein dye was used for scoring and grading at 24 hours, and 7, 14, and 21 days.

Duration of Study

Appendix C is a complete listing of historical events.

Changes/Deviations from the Original Protocol

The initial weighing of the animals was on 23 Feb 88. Hygrothermograph sheets were not available for the two-week period prior to the animals' arrival, since the animals arrived earlier than expected. The lights in Room RS1410 did not cycle properly on 3 March. On 17 March the animals were not fed until 1523 hours. The animals were not given sulfaquinoline and Canex®/mineral oil during their quarantine period. One animal suffered a broken back during dosing due to problems with the animal restrainer. This animal was replaced at the end of the study with 88F046. Animal 88F059 died on day five for reasons not related to the administration of the compound. This animal was not replaced for two reasons: first, the maximum ocular response had already been obtained and second, the cause of death did not appear to affect the ocular response.

Storage of Raw Data and Final Report

A copy of the final report, study protocols, raw data, retired SOPs and an aliquot of the test compound will be retained in the LAIR archives.

TABLE I

GRADES FOR OCULAR LESIONS (4)

CORNEA

Opacity: degree of density (area of greatest density taken for reading)

No ulceration or opacity 0
Scattered or diffuse areas of opacity (other than slight dulling of normal luster), details of iris clearly visible ... 1*

Easily discernible translucent areas, details of iris slightly obscured 2
Nacreous areas, no details of iris visible, size of pupil barely discernible 3
Opaque cornea, iris not discernible through opacity 4

IRIS

Normal 0
Markedly deepened rugae, congestion, swelling, moderate circumiridial hyperemia or injection, any of these or any combination thereof, iris still reacting to light (sluggish reaction is positive) 1*
No reaction to light, hemorrhage, gross destruction (any or all of these) 2

CONJUNCTIVA

Redness: (refers to palpebral and bulbar conjunctiva, excluding cornea and iris)

Blood vessels normal 0
Some blood vessels definitely hyperemic (injected) 1
Diffuse, crimson color, individual vessels not easily discernible. 2*
Diffuse, beefy red 3

Chemosis: lids and/or nictitating membranes

No swelling 0
Any swelling above normal (including nictitating membranes) .. 1
Obvious swelling with partial eversion of lids 2*
Swelling with lids about half-closed 3
Swelling with lids more than half-closed 4

*Indicates minimum level for a positive response

RESULTS

OCULAR SIGNS

Results from scoring the ocular irritation in each rabbit are tabulated in Appendix D.

Opacities occurred in four of the six animals in the No-Wash Group (Appendix D, Table D-1). Opacities were present at four hours and lasted through 24 hours in two animals. An opacity was present in one animal at 24 hours, only. The opacities in the fourth animal persisted through 7 days. This animal also developed pannus (neovascularization of the cornea) which persisted for the duration of the study. No opacities were observed in the animals washed at either 10 or 30 seconds.

Iritis was present in all animals of the No-Wash Group (Appendix D, Table D-2). The symptoms were observed at one hour and persisted for 24 hours in five of the six animals. The iritis in one animal persisted through 72 hours. The iritis resolved more quickly in the Wash-at-30-Seconds Group. Only two animals had unresolved iritis in this group at 24 hours. The iritis had resolved in all of the animals washed at 30 seconds by 48 hours. In the Wash-at-10-Seconds Group, the development of iritis was even less severe. Only three of six animals developed iritis. This had resolved in two animals by four hours and in the last animal by 24 hours.

Animals in all three groups developed conjunctival redness (Appendix D, Table D-3). This was observed at one hour. The No-Wash Group was the most severely affected with two scores of 2 lasting for 72 hours (with a score of 1 at the 1 and 4 hour observations). The Wash-at-30-Seconds Group had scores of 1 lasting through 72 hours. Scores of 2 in this group generally did not persist beyond 4 hours. In the Wash-at-10-Seconds Group, conjunctival redness had resolved in three of six animals by 48 hours. The redness had resolved in an additional two animals by the 72 hours. The redness in one animal persisted with a score of 1 through 7 days.

Chemosis (Appendix D, Table D-4) was observed at one hour in all animals. At four hours, the chemosis was scored as two or greater in all animals of the No-Wash and Wash-at-30-Seconds Groups. Only two animals in the Wash-at-10-Seconds Group developed a score of 2. By 48 hours, the chemosis of three of six animals in the Wash-at-10-Seconds Group had resolved completely. The chemosis of only one animal of the other groups had resolved at this time. Chemosis had resolved in all but one animal of the Wash-at-10-Seconds Group by 72 hours. The chemosis in this animal persisted through 7 days with a score of one. Chemosis

persisted in the other groups through 72 hours (eight of twelve animals).

CLINICAL SIGNS

All six animals of the No-Wash Group developed aqueous flare (Tendall Effect) by the observation at one hour which had resolved in all six animals 48 hours after dosing. Five of six animals in the Wash-at-30-Seconds Group exhibited aqueous flare. It had resolved by the observation at 24 hours. Aqueous flare developed in only one animal of the Wash-at-10-Seconds Group. It was present at the observation at one hour and had resolved prior to the observation at 24 hours. Additional information is presented in Appendix E.

An off-white exudate was present in 17 of 18 animals. This exudate had resolved in 16 of 17 animals by 24 hours. The exudate in the remaining animal had not resolved until 48 hours. The exudate reappeared in one animal at the observation at 48 hours. A clear exudate, of very slight severity, was present in the medial canthi of all six animals in the Wash-at-30-Seconds Group before dosing.

Fluorescein staining of the cornea was observed in all six animals of the No-Wash Group but it was not detected in animals of the other two groups. More information is presented in Appendix E.

Tearing was present in 17 of 18 animals. One animal of the Wash-at-10-Seconds Group did not develop this sign. Tearing had resolved in all of the No-Wash Group by the observation at 72 hours. This sign resolved in all but one animal of the Wash-at-30-Seconds Group by 48 hours after dosing and persisted in the remaining animal of this group through the observation at 48 hours. The tearing in four of the five animals in the Wash-at-10-Seconds Group which developed this sign had resolved prior to the observation at 24 hours. Tearing in one animal persisted through the observation at 24 hours.

Only the six animals of the Wash-at-30-Seconds Group became photophobic. The photophobia had resolved in all six animals prior to the observation at 24 hours.

Neovascularization of the cornea occurred in one animal (88F058) of the No-Wash Group. It first appeared at the observation at seven days and persisted throughout the study.

One animal (88F059) displayed diarrhea and malaise and did not eat. This rabbit was found with one foot caught between the cage and cage floor four days after dosing. During examination on the fifth day after dosing the animal expired. Necropsy findings were lesions indicative of

hepatic and omental abscesses, urinary tract stasis with ruptured bladder, and mucoid enteropathy. The changes in this animal were the only abnormalities found at necropsy (Appendix F).

DISCUSSION

The results of this study indicate that LP1846 is a strong ocular irritant which produces temporary corneal opacities for up to a week in addition to iritis, conjunctival redness, and chemosis. This is not surprising as LP1846 contains hydroxylammonium nitrate, the nitrate salt of hydroxylamine which has been reported to be a potent dermal irritant (6). The data do indicate, however, that LP1846 is an irritant rather than a corrosive (irreversible) compound in that all the toxicity associated with LP1846 exposure had cleared within 21 days.

Washing with tap water effectively reduced the ocular toxicity associated with LP1846 exposure. Washing at 30 seconds after exposure eliminated the corneal opacity and significantly reduced the severity and duration of the iritis, chemosis, and conjunctival redness as compared to the No-Wash Group results. In an attempt to eliminate these signs of ocular irritation, the eyes were washed only 10 seconds after exposure. There was a further reduction in severity and duration of the iritis, chemosis, and conjunctival redness consistent with a reduced period of exposure to the LP1846, but the signs of ocular irritation were not eliminated. In fact, the responses obtained in the Wash-at-10-Seconds Group would still be classified as a positive response under EPA health effects test guidelines for ocular irritation testing (4).

Although the ocular toxicity associated with LP1846 exposure is temporary, the accidental exposure of a weapon's crew member has the potential to reduce the combat effectiveness of the crew for up to a week. This prognosis is based on the assumption that reduced combat effectiveness would be most closely associated with corneal opacities. Wearing of protective equipment (goggles) would eliminate the risk of ocular toxicity, but use of protective equipment in the field situation is not absolute. Thus, the efficacy of washing even 30 seconds after exposure in eliminating the corneal opacities and alleviating the other signs of ocular toxicity means that routine first-aid procedures would essentially eliminate any reduction in combat effectiveness if accidental exposure were to occur.

CONCLUSIONS

The liquid propellant LP1846 is an ocular irritant according to EPA criteria. Washing the eye at 30 seconds alleviated the conjunctival and iritic symptoms and prevented the development of corneal lesions. Immediate washing at 10 seconds after dosing was even more successful in alleviating the symptoms. However, LP1846 would still be classified as an irritant under the wash conditions.

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3. Siegel J. Monopropellants; toxicological evaluation of. Bethesda, MD: U.S. Navy Toxicology Unit, National Naval Medical Center; August 1970.

4. Environmental Protection Agency. Office of Pesticides and Toxic Substances, Office of Toxic Substances (TS-792). Primary Eye Irritation. In: Health effects test guidelines. Washington, DC: Environmental Protection Agency, August 1982; EPA 560/6-82-001.

5. Primary Eye Irritation Study. LAIR Standard Operating Procedure OP-STX-33. Presidio of San Francisco, CA: Letterman Army Institute of Research; 15 June 1984.

6. Windholz W., ed. Merck Index. 10th ed. Rahway, NJ: Merck and Co., 1983: 703.

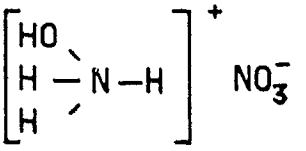
APPENDIX A: CHEMICAL DATA

Chemical name: Liquid Gun Propellant 1846 (LP1846)

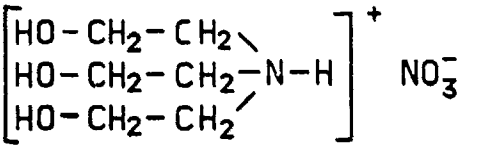
Lot Number: 50-4

LAIR Code: TP69

Chemical Structures:



HAN



TEAN

Molecular Formula: HAN: $H_4N_2O_4$, TEAN: $C_6H_{16}N_2O_6$

Molecular Weight: HAN: 96.04, TEAN: 211.19

Analytical Data:

LP1846 was analyzed by titration with a standardized alcoholic solution of potassium hydroxide using a procedure supplied by Charles Leveritt.[1] This yielded the sum of the HAN and TEAN components. Titration of the propellant after heating with benzaldehyde provided the concentration of HAN alone. Analysis of the compound in this laboratory gave the following composition:[2]

HAN	60.5%
TEAN	18.4%
Water	20.1%

Source: Charles S. Leveritt
Advanced Ballistic Concepts Branch
Interior Ballistic Division
US Ballistics Research Laboratory
Aberdeen Proving Ground, MD

---

[1] Leveritt, CS. [Letter]. SUBJECT: Analysis of liquid propellants by titration (15 April 1986). Aberdeen Proving Ground, Maryland: US Army Laboratory Command, Ballistic Research Laboratory.

[2] Wheeler, CR. Toxicity testing of propellants. Laboratory Notebook #85-12-023.2, pp 17-23. Letterman Army Institute of Research, Presidio of San Francisco, CA.

APPENDIX B: ANIMAL DATA

Species: *Oryctolagus cuniculus*

Strain: New Zealand White (albino)

Source: Hazleton Research Products, Inc.
P.O. BOX 7200, Denver, PA 17517

Sex: Male

Age: Young Adults

Animals in each group: 6 males

Condition of animals at start of study: Normal

Body weight range at dosing: 2.6 to 3.4 kg

Identification procedures: Animal numbers written in indelible ink in the ear. Animal numbers: 88F046 to 88F053, 88F055, 88F057 to 88F061, and 88F063 to 88F066.

Pretest conditioning:

1. Quarantine from 18 February to 29 February 1988

2. Animal eyes were evaluated 24 hours before dosing by visual examination, reexamined with a slit lamp, and with uv light after application of fluorescein dye.

Justification: Laboratory rabbits are a proven sensitive animal model for ocular testing.

APPENDIX C: HISTORICAL LISTING OF STUDY EVENTS

Date	Event
18 Feb 88	Animals arrived at LAIR.
18 Feb - 5 Apr 88	Animals were checked daily.
23 Feb 88	Animals were weighed.
29 Feb 88	Animals were removed from quarantine and weighed. Animals in Group 30S (Wash-at-30-Seconds Group) were checked for preexisting ocular injury.
1 Mar 88	Group 30S animals were dosed. Observations at 1 and 4 hours were conducted.
2 Mar 88	Post-exposure scores were performed for group 30S at 24 hours.
3 Mar 88	Post-exposure scores were performed for group 30S at 48 hours.
4 Mar 88	Post-exposure scores were performed for group 30S at 72 hours.
7 Mar 88	All animals were weighed. Animals in Group N (No-Wash Group) were checked for preexisting ocular injury.
8 Mar 88	Group N animals were dosed (except for 88F046). Observations were conducted at 1 and 4 hours. Group 30S was scored at 7 days.
9 Mar 88	Group N was scored at 24 hours.
10 Mar 88	Group N was scored at 48 hours.
11 Mar 88	Group N was scored at 72 hours.
14 Mar 88	All animals were weighed. Animals in Group 10S (Wash-at-10-Seconds Group) were checked for preexisting ocular injury.
15 Mar 88	Group 10S animals were dosed. Observations were conducted 1 and 4 hours after dosing. Group 30S 14-day scores were performed. Group N was scored at 7 days.

16 Mar 88	Group 10S was scored at 24 hours. Group 30S was taken to necropsy.
17 Mar 88	Group 10S was scored at 48 hours.
18 Mar 88	Group 10S was scored at 72 hours.
21 Mar 88	All animals were weighed.
22 Mar 88	Group N was scored at 14 days. Group 10S was scored at 7 days. Five animals of Group 10S sent to necropsy.
28 Mar 88	All animals were weighed. Animal 88F046 was given a pre-exam.
29 Mar 88	Animal 88F046 was dosed. Observations at 1 and 4 hours were performed. Group N was scored at 21 days. Group N was taken to necropsy. Remaining animal in Group 10S was scored at 14 days. Remaining animal in Group 10S was taken to necropsy.
30 Mar 88	Animal 88F046 was scored at 24 hours.
31 Mar 88	Animal 88F046 was scored at 48 hours.
1 April 88	Animal 88F046 was scored at 72 hours.
5 April 88	Animal 88F046 was scored at 7 days and was taken to necropsy.

APPENDIX D: INDIVIDUAL IRRITATION SCORES

TABLE D-1

EFFECT OF A WASHING ON OPACITY SCORES

FOLLOWING INSTILLATION OF LP1846 IN RABBIT EYES

	ANIMAL #	PRE	1 HR	4 HR	24 HR	48 HR	72 HR	7 DA	14 DA	21 DA
NO WASH	88F046	0	0	0	0	0	0	0	S*	S
	88F053	0	0	1	1	0	0	0	0	0
	88F057	0	0	0	0	0	0	0	0	0
	88F058	0	0	1	1	3	3	2	0	0
	88F059	0	0	0	1	0	0	S	S	S
	88F060	0	0	1	1	0	0	0	0	0
WASH AT 10 SECONDS	88F047	0	0	0	0	0	0	0	S	S
	88F048	0	0	0	0	0	0	0	S	S
	88F049	0	0	0	0	0	0	0	S	S
	88F050	0	0	0	0	0	0	0	S	S
	88F051	0	0	0	0	0	0	0	S	S
	88F052	0	0	0	0	0	0	0	0	S
WASH AT 30 SECONDS	88F055	0	0	0	0	0	0	0	0	S
	88F061	0	0	0	0	0	0	0	0	S
	88F063	0	0	0	0	0	0	0	0	S
	88F064	0	0	0	0	0	0	0	0	S
	88F065	0	0	0	0	0	0	0	0	S
	88F066	0	0	0	0	0	0	0	0	S

*S indicates that the animal was sacrificed following the previous observation.

TABLE D-2

EFFECT OF A WASHING ON IRITIS SCORES

AFTER INSTILLATION OF LP1846 IN RABBIT EYES

	ANIMAL #	PRE	1 HR	4 HR	24 HR	48 HR	72 HR	7 DA	14 DA	21 DA
NO WASH	88F046	0	1	1	0	0	0	0	S*	S
	88F053	0	1	1	1	0	0	0	0	0
	88F057	0	1	1	1	0	0	0	0	0
	88F058	0	1	2	1	1	1	0	0	0
	88F059	0	1	1	1	0	0	S	S	S
	88F060	0	1	1	1	0	0	0	0	0
WASH AT 10 SECONDS	88F047	0	0	0	0	0	0	0	S	S
	88F048	0	0	0	0	0	0	0	S	S
	88F049	0	1	1	0	0	0	0	S	S
	88F050	0	0	0	0	0	0	0	S	S
	88F051	0	1	0	0	0	0	0	S	S
	88F052	0	1	0	0	0	0	0	0	S
WASH AT 30 SECONDS	88F055	0	1	1	1	0	0	0	0	S
	88F061	0	1	1	0	0	0	0	0	S
	88F063	0	1	1	0	0	0	0	0	S
	88F064	0	1	1	0	0	0	0	0	S
	88F065	0	1	1	0	0	0	0	0	S
	88F066	0	1	1	1	0	0	0	0	S

*S indicates that the animal was sacrificed following the previous observation.

TABLE D-3

EFFFECTS OF A WASHING ON CONJUNCTIVAL REDNESS SCORES FOLLOWING INSTILLATION OF LP1846 IN RABBIT EYES

	ANIMAL #	PRE	1 HR	4 HR	24 HR	48 HR	72 HR	7 DA	14 DA	21 DA
NO WASH	88F046	1	2	2	2	2	1	0	S*	S
	88F053	1	1	1	2	2	2	1	0	0
	88F057	0	1	1	2	1	1	0	1	0
	88F058	0	1	1	2	2	2	0	1	1
	88F059	0	1	1	2	2	1	S	S	S
	88F060	0	2	2	2	1	1	1	1	1
WASH AT 10 SECONDS	88F047	0	1	2	1	0	0	0	S	S
	88F048	0	1	2	1	0	0	0	S	S
	88F049	0	2	2	1	1	0	0	S	S
	88F050	0	1	2	1	0	0	0	S	S
	88F051	0	1	2	1	1	0	0	S	S
	88F052	0	1	1	1	1	1	1	0	S
WASH AT 30 SECONDS	88F055	0	2	1	1	1	1	0	0	S
	88F061	1	2	1	1	1	1	0	0	S
	88F063	0	2	1	1	1	1	0	0	S
	88F064	0	2	1	1	1	1	0	0	S
	88F065	0	2	1	1	1	1	0	0	S
	88F066	0	2	1	2	1	1	0	0	S

*S Indicates that the animal was sacrificed following the previous observation.

TABLE D-4

EFFECT OF A WASHING ON CHEMOSIS SCORES

FOLLOWING INSTILLATION OF LP1846 IN RABBIT EYES

	ANIMAL #	PRE	1 HR	4 HR	24 HR	48 HR	72 HR	7 DA	14 DA	21 DA
NO WASH	88F046	0	2	2	2	1	0	0	S*	S
	88F053	0	2	2	1	1	1	0	0	0
	88F057	0	1	3	1	1	0	0	1	0
	88F058	0	1	3	3	2	2	0	1	1
	88F059	0	2	2	3	2	1	S	S	S
	88F060	0	2	2	3	1	0	1	1	1
WASH AT 10 SECONDS	88F047	0	2	2	0	0	0	0	S	S
	88F048	0	1	1	0	0	0	0	S	S
	88F049	0	2	2	1	1	0	0	S	S
	88F050	0	1	1	1	0	0	0	S	S
	88F051	0	1	1	1	1	0	0	S	S
	88F052	0	1	1	1	1	1	1	0	S
WASH AT 30 SECONDS	88F055	0	2	3	1	1	0	0	0	S
	88F061	1	2	2	1	0	0	0	0	S
	88F063	0	2	2	2	1	1	0	0	S
	88F064	0	2	2	2	1	1	0	0	S
	88F065	0	2	2	2	1	1	0	0	S
	88F066	1	2	3	2	1	1	0	0	S

*S Indicates that the animal was sacrificed following the previous observation.

APPENDIX E

EFFECT OF A WASHING ON CLINICAL SIGNS

FOLLOWING INSTILLATION OF LP1846 IN RABBIT EYES

	ANIMAL #	PRE	1 HR	4 HR	24 HR	48 HR	72 HR	7 DA	14 DA	21 DA
NO WASH	88F046		A,E,T	A,E,T	T,F	T			S*	S
	88F053		A,T	E	F	F				
	88F057		A,T	A,E,T	T,F					
	88F058		A,T	A,T	A,T,F	T,F	F	N	N	N
	88F059	E	A,T	E,T	F,T	E,F,T		S	S	S
	88F060		A,T	E,T	F	F				
WASH AT 10 SECONDS	88F047		E,T	E,T					S	S
	88F048		E,T	E,T					S	S
	88F049		A,T	A,E,T					S	S
	88F050			E					S	S
	88F051		E,T	E,T	T				S	S
	88F052		E	E,T						S
WASH AT 30 SECONDS	88F055	E	A,T,P	A,E, T,P						S
	88F061	E	T,P	A,E, T,P						S
	88F063	E	A,T,P	A,E, T,P	T	T				S
	88F064	E	A,T,P	E,T,P	T					S
	88F065	E	T,P	E,T,P	T					S
	88F066	E	A,T,P	A,E,T	E,T					S

A = Aqueous Flare
E = Exudate
F = Fluorescein Stain
P = Photophobic
N = Neovascularization
T = Tearing

*S Indicates that the animal was sacrificed following the previous observation.

Appendix F

Pathology Report

Ocular Irritation
GLP 86006

I. Compound: Liquid Gun Propellant LP 1846.
Species: Oryctolagus cuniculus, New Zealand White, adult.

II. Principal Investigator: SSG James D. Justus
Pathologist: MAJ Charles B. Clifford

III. Comment: Except for 1 animal, no gross lesions were observed. No evidence of direct tissue damage due to Liquid Gun Propellant LP1846 was observed in any animal.

Animal #88F059 (accession #42944) had gross and microscopic lesions indicative of hepatic and omental abscesses, urinary tract stasis with ruptured urinary bladder, and mucoid enteropathy. All lesions in this animal are considered incidental findings.

CHARLES B. CLIFFORD, DVM
MAJ, VC
Division of Pathology

1 August 1988/dbj

GLP 86006

Attachment:

Group 1: No wash - All males

Animal ID	LAIR Acc #	Necropsy Date	Diagnosis
88F046	43027	05 Apr 88	No lesions recognized
88F053	42987	29 Mar 88	No lesions recognized
88F057	42986	29 Mar 88	No lesions recognized
88F058	42985	29 Mar 88	No lesions recognized
88F059	42944	15 Mar 88	Ruptured bladder and hepatic abscesses
88F060	42989	29 Mar 88	No lesions recognized

Group 2: Wash at 30 seconds. All males

88F055	42956	16 Mar 88	No lesions recognized
88F061	42957	16 Mar 88	No lesions recognized
88F063	42958	16 Mar 88	No lesions recognized
88F064	42959	16 Mar 88	No lesions recognized
88F065	42960	16 Mar 88	No lesions recognized
88F066	42961	16 Mar 88	No lesions recognized

Group 3: Wash at 10 seconds. All males

88F047	42965	22 Mar 88	No lesions recognized
88F048	42966	22 Mar 88	No lesions recognized
88F049	42967	22 Mar 88	No lesions recognized
88F050	42968	22 Mar 88	No lesions recognized
88F051	42969	22 Mar 88	No lesions recognized
88F052	42988	29 Mar 88	No lesions recognized

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